EDITORIAL COMMENT†

DUPLEX ANTIGENS

Data, suggesting that a single protein molecule may stimulate the production of two qualitatively-different circulating antibodies, are currently reported by Smadel[1] and his coworkers of the Rockefeller Institute.

It was shown by Tanaka[2] and Freyer,[3] in 1902-4, that vaccine lymph gives specific flocculation reactions with vaccinia-immune serum. Two soluble antigens were afterwards demonstrated in this lymph[4]: a heat-labile (L) antigenic fraction readily destroyed at 56°C., and a heat-stable (S) fraction resisting heat to 95°C. By cross-absorption tests, Cragie[5] afterwards demonstrated that the same L- and S-antigens are also present in vaccine elementary bodies. There was suggestive evidence that the L- and S-antigens are conjugated, in the elementary body, to form a single protein complex, the so-called "LS-antigen," which is capable of reacting equally well with L- and S-circulating antibodies. It was suggested by Smadel and Rivers[1] that the serologically-active parts of this hypothetical protein conjugate (LS) undergo a series of independent degradations, giving rise to such fractionally-denatured complexes as L'S, L"S, LS', L'S', etc.

This theory of the nature of the natural antigen in elementary bodies is currently tested on vaccine dermal filtrates by the Rockefeller biochemists. Dermal pulp, from cutaneously infected rabbits, was extracted in a 1:50 dilution of standard phosphate buffer solution (pH 7.2). The extract was afterwards freed from cellular débris by centrifugation, followed by Seitz filtration. Electrophoretic analysis of the resulting filtrate demonstrated the existence of four distinct protein fractions. Fractionation was effected by altering the pH of the filtrate, by which means the dermal proteins were separated into three overlapping groups: A, proteins which remained in solution at pH 4.63; B, proteins precipitated at pH 4.63, but soluble at pH 6.31; and C, proteins precipitated at pH 6.31, but soluble at pH 8.56. On reprecipitation both A and C fractions were serologically inert, giving no test-tube reactions with either L- or S-antibody. The original reacting titer of the dermal filtrate, however, was found quantitatively in the B fraction. Physical and chemical studies showed this fraction to be a homogeneous protein, with a molecular weight approximately that of serum globulin. This B-protein is precipitated quantitatively with either L- or S-precipitin, from which they conclude that this natural antigen is "a single molecular substance containing both L- and S-activity."

They found that the L-portion of this native antigen can be partially (L') or completely (L") denatured by heat, without serological alteration of the S-portion. By means of enzymic digestion, the S-portion can be similarly degraded (S', S") without demonstrable alteration of the L-portion. Dissociation of the LS-molecule into free L- and free S-antigen, however, was not demonstrated, the allegedly free L- and S-antigens of previous investigators presumably being L"S, LS", or other unipolar degeneration products.

Demonstration of this duplex antigenic protein is not only a valuable contribution to the current theory of acquired immunity to vaccine virus, but is equally suggestive in numerous other infectious and allergic processes. Thus far allergists, for example, have almost invariably reasoned from the assumed one-to-one, antigen-antibody relationships of classical immunology, in spite of the reported synthesis of numerous "duplex" proteins of "hybrid" antigenicity.[6] For a decade the "emergent evolution" of new or "hybrid" blood specificities has been of speculative interest to geneticists.[7] The dual antigenic molecule of the Rockefeller biochemists, therefore, may also be of basic nonclinical biological interest.

P. O. Box 51.

W. H. MANWARING,
Stanford University.

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MALPRACTICE PROPHYLAXIS—MEDICAL DEFENSE*

A reduction in the number of malpractice actions can be effected only through the development of a strong defense. It is obvious that such actions would be discouraged if plaintiffs consistently failed to obtain favorable judgments.

Of course, it is not to be argued that a doctor who is actually guilty of malpractice should be allowed to go free of any penalty. There are meritorious claims, and these should be settled out of court—preferably before suit has been filed.

Unjustifiable claims, however, should be contested as thoroughly as possible. In such cases it is sheer folly to compromise, on the theory that a slight settlement would be less expensive than the cost of defense. Such a course serves as an

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* Third of a series of articles on Malpractice Prophylaxis (Article I, in July issue, on page 7. Article II, in August, on page 121.)